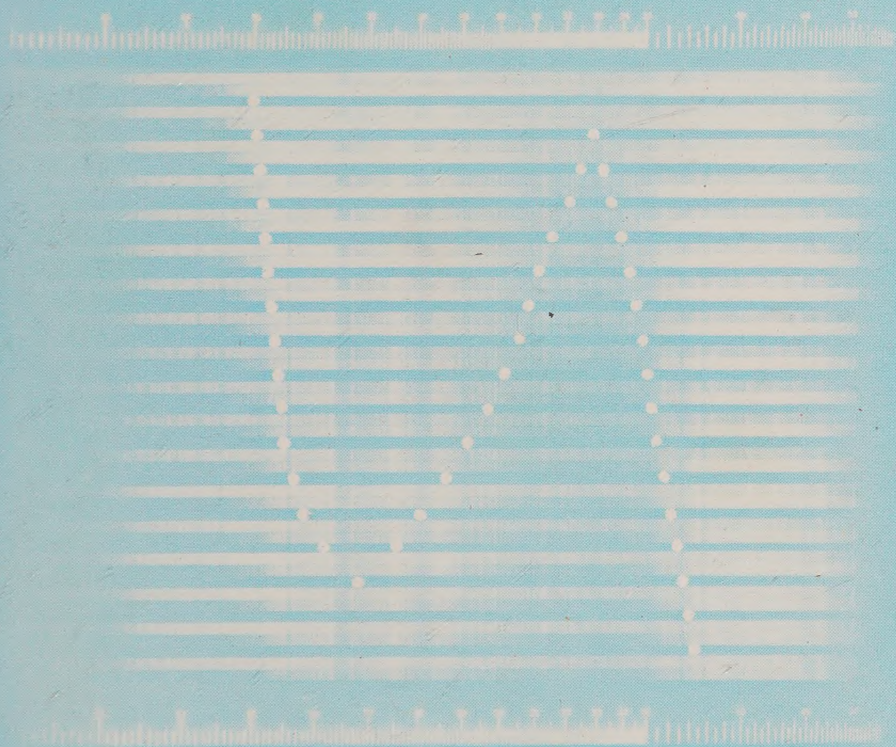


# The Vitamins

An epitome of  
contemporary knowledge



**A spectrogram**

## **THE CROOKES LABORATORIES**

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## Prefatory Note

**T**HE interest of the medical profession in the subject of vitamins, and their great importance in nutrition, was made so gratifyingly evident by the reception accorded to the brochure "A Vitamin Survey" that The Crookes Laboratories decided to issue the present publication entitled :

### **"THE VITAMINS"**

It is hoped that this further effort—a revised and enlarged edition of its predecessor—will prove even more useful, inasmuch as it embraces the latest available findings in a field of intensive research in which no insignificant part has been and continues to be played by

THE CROOKES LABORATORIES

# PLATE I

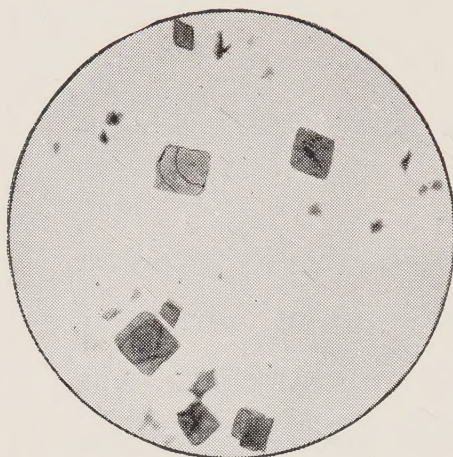


fig. 1.  $\beta$ -CAROTENE  $\times 200$

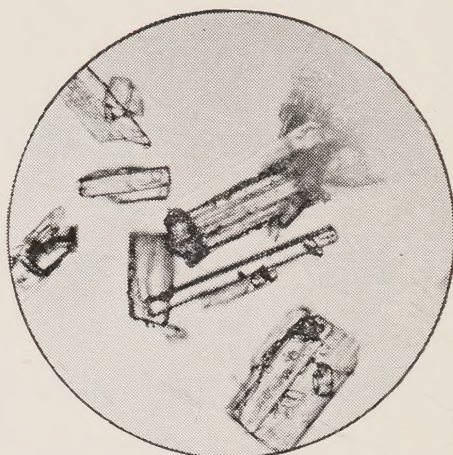


fig. 2. CALCIFEROL  $\times 120$



fig. 3. ANEURIN ( $B_1$ )  $\times 650$

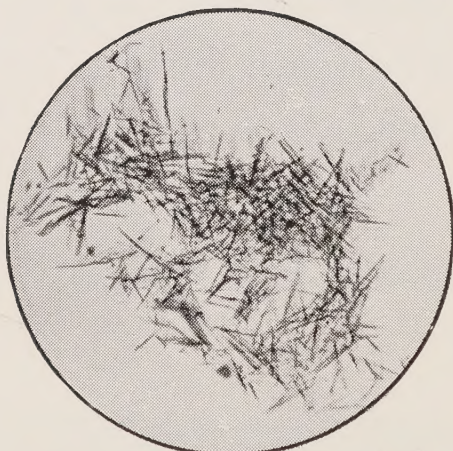


fig. 4. RIBOFLAVIN ( $B_2$ )  $\times 650$

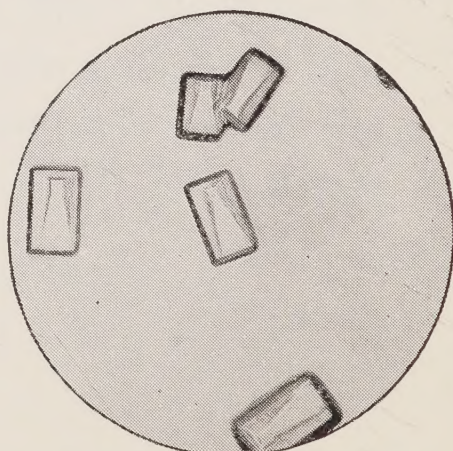


fig. 5. ASCORBIC ACID  $\times 120$

# THE VITAMINS

**R**ATHER more than a quarter of a century ago the existence and the importance of the vitamins was first clearly demonstrated. In many quarters the significance of the discovery was not recognised for a long time. Moreover, many authorities questioned the existence of the vitamins as definite chemical substances, whilst others were reluctant to believe that the results of laboratory experiments had any direct bearing on the nutritive disorders of man. Time has greatly changed the outlook. Orr's survey of our English diets \* has revealed that under-nourishment in respect to vitamins is far more common than was ever suspected, whilst those who thought of the vitamins as indefinite, perhaps even hypothetical, factors are now confounded by the sight of no less than eight pure chemical substances isolated, all of known chemical constitution. Six of them have actually been synthesised by the brilliant achievements of modern organic chemistry.

## How Many Vitamins Exist?

Students of experimental animal nutrition have satisfactorily differentiated fifteen factors which can be classified as vitamins. Of these, ten are known to be concerned in human nutrition ; possibly others are also of importance to man, but this has not yet

\* "*Food, Health and Income*," London, 1936.

been established. The more exact the studies of the requirements of the animal organism become, the more is one impressed by their complexity. In all probability many factors await discovery.

## FAT SOLUBLE VITAMINS

|                                                                                                                                      | <i>See page</i> |
|--------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| <b>A<sub>1</sub></b> Also termed the anti-xerophthalmic or anti-infective factor.....                                                | 5               |
| <b>A<sub>2</sub></b> Probably closely related physiologically to A <sub>1</sub> .....                                                | 6               |
| <b>D<sub>2</sub></b> Calciferol, the artificial product of the ultra-violet irradiation of ergosterol                                |                 |
| <b>D<sub>3</sub></b> Natural vitamin D, as isolated from high-potency liver oils—now known to contain several anti-rachitic factors. | 11-17           |
| <b>E</b> Anti-sterility factor .....                                                                                                 | 18              |
| <b>K</b> Anti-hæmorrhagic vitamin concerned with blood-clotting .....                                                                | 20              |

## WATER SOLUBLE VITAMINS

|                                                                                                                             | <i>See page</i> |
|-----------------------------------------------------------------------------------------------------------------------------|-----------------|
| <b>B<sub>1</sub></b> Anti-neuritic. Beri-beri preventive factor                                                             | 22              |
| <b>B<sub>2</sub></b> Now generally referred to as Riboflavin, It is concerned with oxidising mechanisms in the tissues..... | 27              |
| <b>B<sub>3</sub></b> } Growth factors detected in certain animal                                                            |                 |
| <b>B<sub>4</sub></b> } experiments but their relation to human                                                              |                 |
| <b>B<sub>5</sub></b> } nutrition is not yet clearly defined.                                                                | —               |
| <b>B<sub>6</sub></b> Rat anti-dermatitis factor .....                                                                       | —               |
| <b>P.P</b> Factor. Nicotinic acid or Nicotinamide. Anti-pellagra factor .....                                               | 30              |
| <b>C</b> Ascorbic Acid. Anti-scorbutic factor.....                                                                          | 33              |
| <b>P</b> Citrin. A factor associated with ascorbic acid and believed to supplement its action.....                          | 38              |

# Descriptive Details of Vitamins

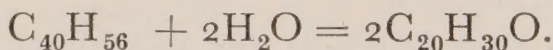
## VITAMIN A<sub>1</sub>

Anti-Xerophthalmic and  
Anti-Infective Factors

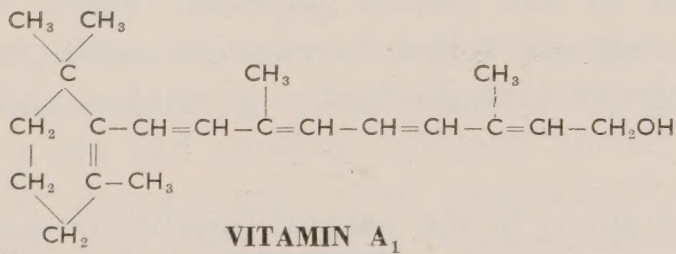
This substance, found in many animal tissues, particularly in liver, arises

from the breakdown of a well-known plant pigment,  $\beta$ -carotene. The latter is, therefore, usually referred to as pro-vitamin A. Carotene is a hydro-carbon  $C_{40}H_{56}$  found in all green plant tissues and in certain roots and fruits (*e.g.*, carrots and the flesh of palm fruits). See Fig. 1, page 2.

In the animal body, probably in the liver, it is broken down according to the equation :—



The alcohol  $C_{20}H_{30}O$  is vitamin A<sub>1</sub>. It is a pale yellow, viscous oil, of which the chemical constitution is :—



It has recently been synthesised, but synthetic material is not yet available for therapeutic use.

*See also References on pages 40-42.*

Vitamin A<sub>2</sub>

This compound closely resembling vitamin A<sub>1</sub> in chemical character was recently discovered in the liver oils of fresh water fishes. It has not yet been fully identified, but it is probable that it has a biological activity similar to that of vitamin A<sub>1</sub>.

Yet another vitamin A-like substance is found in the liver oil of the whale. It is probably of similar constitution to vitamin A<sub>1</sub>, but containing a side chain of nine carbon atoms instead of eleven. It is distinguishable from vitamin A<sub>1</sub> by the position of its absorption band in the ultra-violet region of the spectrum. Its biological activity is at present unknown.

## Physiological Effect

Vitamin A is probably the physiologically active agent, but carotene and the vitamin produce the same effect when administered. The absorption of the vitamin from the intestine is usually more satisfactory than that of the parent pigment, hence a more prompt response follows treatment with materials containing the vitamin itself, *e.g.*, high-potency liver oils.

Some others of the natural lipochrome pigments, *e.g.*,  $\delta$ -carotene and kryptoxanthine, also give rise to vitamin A in the animal body. They are not, however, so important as  $\beta$ -carotene ; in the first place, because they are less common, and secondly, because they form only half the amount of A<sub>1</sub>.

### Essential for Satisfactory Growth

An adequate supply of vitamin A in the diet is essential for satisfactory growth in childhood and for the maintenance of a normal resistance against infection both in youth and in adult life. The experimental work of Mellanby and Green showed in a striking manner the lowering of the resistance against bacterial infection which occurs when the diet is deficient in vitamin A. The observations made in this study have been applied to human cases with very promising results.

The characteristic change seen in the tissues of individuals who have been deprived of vitamin A is a keratinisation of the epithelial structures. This may occur very extensively. It is particularly the line of defence against infection, represented by the epithelial tissues, that suffers in vitamin A deprivation.

In prolonged cases of deficiency the cutaneous epithelium may be so extensively keratinised as to give rise to a dry and atrophic condition known as “toad skin” or phrynoderma. This complaint is often seen in Ceylon and China, but it is comparatively rare in Western Europe. Milder forms showing a dry skin and slight keratinisation are, however, more common than is usually suspected.

*See also References on pages 40-42.*

### Xerophthalmia

It is now widely recognised that deficiency of vitamin A plays a large part in the causation of xerophthalmia.

Mild cases of this condition are sometimes met with in ordinary practice. They respond immediately to treatment with vitamin-A-rich preparations, *e.g.*, halibut liver oil.

### Night Blindness

Another recent discovery is that a considerable proportion of apparently normal individuals show a slightly defective power of adaptation to dim illumination. This condition appears to be a mild form of night-blindness, which is now generally recognised as due to A-deficiency. Treatment of the mild or the severe form of this disturbance with vitamin A brings about a rapid improvement. It has been experimentally demonstrated that the vitamin plays a direct *rôle* in the cycle of bleaching and regeneration of visual purple in the retina.

### Dark Adaptation as a Test for Vitamin A Deficiency

So well marked is this symptom of vitamin A deficiency that it is now largely used as a convenient method for detecting this condition amongst different sections of the population.

Recent studies have shown that 30 per cent. of the children in poorer-class districts show this symptom of vitamin A deficiency.

There are good grounds for believing that impaired adaptation to dim light is responsible for a proportion of motor accidents at night-time.

## Human Requirements

Estimates of vitamin A should always be expressed in terms of the International Units defined by the Health Organisation of the League of Nations. There appear to be good grounds for believing that the requirements are of the order of 75 International Units daily per kilogram of body weight. Thus, for example :—

|                        |      |     |       |                     |
|------------------------|------|-----|-------|---------------------|
| 3 months' infant ..... | 6    | kg. | 450   | International Units |
| 10 „ „ .....           | 10   | kg. | 750   | „ „                 |
| Child of 5 stone ..... | 31.5 | kg. | 2,400 | „ „                 |
| Adult of 10 „ .....    | 63   | kg. | 4,800 | „ „                 |

The League of Nations Technical Commission advises daily intakes of 2,000–4,000 International Units for adults ; 6,000–8,000 for growing children and 5,000 for pregnant women.

### Modern Dietary Deficiency

Many modern diets are defective in that they supply only about 700–1,000 units for an adult. When deficiency is suspected, as much as 40,000–100,000 units a day can be given for a time without fear of excess. The vitamin A contents of important foods are given in the table on next page.

*See also References on pages 40–42.*

## Vitamin A content of Foods

| International Units per gm. or ml. |                   |
|------------------------------------|-------------------|
| Milk . . . .                       | 3-5               |
| Butter . . .                       | 20-50, average 40 |
| Egg Yolk                           | 50                |
| Spinach                            | 50                |
| Carrots . .                        | 19                |
| Cabbage                            | 9                 |
| Runner<br>beans                    | 6                 |

fresh or  
boiled.

The values in the left-hand column can be contrasted with the following:  
International Units per gm.

|                               |           |
|-------------------------------|-----------|
| Pure Vitamin A                | 2,560,000 |
| Cod Liver Oils                | 600-3,000 |
| Crookes' Cod<br>Liver Oil     | 2,000     |
| Crookes' Halibut<br>Liver Oil | 52,000    |

### Seasonal Variation in Value

It is particularly important to remember that there are seasonal variations in the vitamin A value of dairy produce, which are reflections of the seasonal changes in the feeding of farm stock. Generally speaking, the vitamin A values of milk, butter and eggs tend to be at their lowest in the early part of the year and to be at their highest in the months of June and July. There can be little doubt that the marked increase in the incidence of ill-health which is associated with the early months of the year is related to these seasonal variations in the vitamin content of foods.

## VITAMIN D

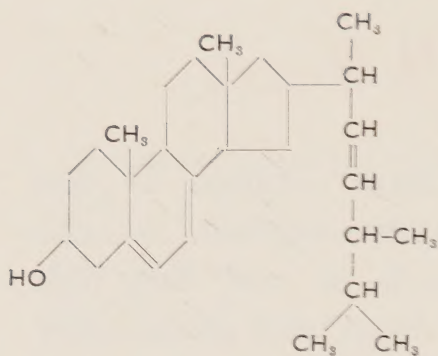
### Anti-Rachitic Factor

The term vitamin D was originally applied to the substance present in oils, such as cod liver oil, which for many years past have been used medicinally for their anti-rachitic properties. It was believed to be identical with the compound known as calciferol, which is produced from ergosterol by irradiation with ultra-violet light. A very simple relationship was then traced between the three methods of treating rickets. If the child was treated directly by ultra-violet irradiation one assumed that ergosterol in the skin was converted into the active compound calciferol and that this passed into the circulation and influenced calcium and phosphate retention. Alternatively, the rachitic infant could be given calciferol or preparations of irradiated "activated" materials. A third method was to administer products such as cod liver oil or more potent fish liver oils, it being again assumed that these owed their potency to the presence of calciferol.

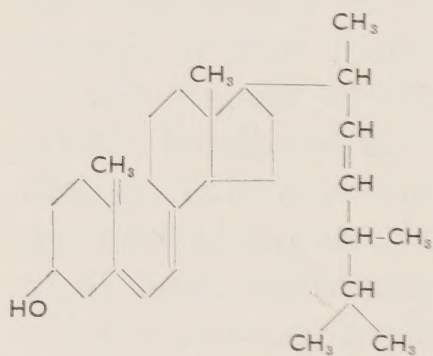
### Natural versus Artificial Vitamin

This point of view was seriously disturbed when evidence began to accumulate, showing that the anti-rachitic agent in fish liver oils is not identical with the product of the artificial irradiation of ergosterol. Moreover, there were

*See also References on pages 40-42.*

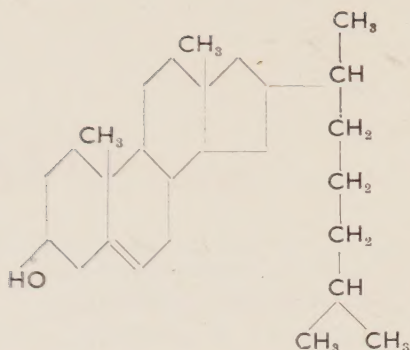


**ERGOSTEROL**

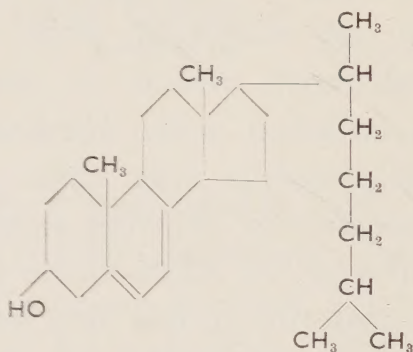
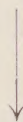


**CALCIFEROL**

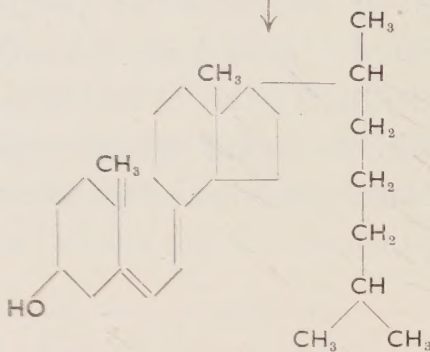
**VITAMIN D<sub>2</sub>**



**CHOLESTEROL**



**7-8 DEHYDRO-CHOLESTEROL**



**NATURAL VITAMIN D**

**VITAMIN D<sub>3</sub>**

*N.B.*—The appellation D<sub>1</sub> was given to a product which later proved to be impure. It is now obsolete.

some indications that the natural vitamin D is more potent in facilitating calcification than the artificial laboratory product calciferol. This work has led to the isolation of natural vitamin D, or one of the natural D factors, for it seems that several may exist. It appears to be chemically related to cholesterol in the same manner as calciferol is related to ergosterol. *See Fig. 2, page 2 ; also graphic formulæ, page 12.*

It can be made artificially by irradiating the compound 7.8 dehydro-cholesterol, which can be made in the laboratory from cholesterol.

### Physiological Action

Both natural vitamin D and calciferol appear to act by favouring the retention of bone-forming salts in the body. Calcium and phosphates are often absorbed by the rachitic child but are re-excreted, so that a negative balance results. Vitamin D prevents the loss by re-excretion into the lumen of the gut and thus creates more favourable conditions for calcification of growing bone. It is not known how this effect is produced, but there are some observations to show that the vitamin produces a change in the reaction of the contents of the gut which favours absorption and retention of bone-forming minerals.

Recent work shows that it is particularly concerned with absorption of phosphates.

*See also References on pages 40-42.*

## Human Requirements

For infants up to 6 months of age doses of from 1,000 to 2,000 International Units are suggested. Older children can be given 2,000–5,000 units without hesitation during the period of rapid growth. Smaller doses, 200–500, are indicated for adults, but their actual requirements are not yet known with any certainty. It is nearly always advisable to supplement the treatment by increasing the intake of calcium and phosphates.

It is not sufficiently recognised that our modern diets are, with few exceptions, inadequate in both respects. Orr's survey of the diets of the English population showed that the poorest section of the community takes, on an average, only 0.37 g. calcium and 0.81 g. of phosphorus daily, whilst the best-fed class studied consumed foods supplying respectively 0.95 g. calcium and 1.54 g. phosphorus. Opinion is coming round to the view that an intake of not less than 1.5 g. calcium and 2.0 g. phosphorus is desirable for adults, and that the requirements during childhood and growth are not much less.

### Oral Administration Advisable

The administration should in general be by the oral route, as it has been shown that the response is much more rapid than when the material is introduced subcutaneously or by inunction.

## The Sources

As the table below shows there are very few ordinary foods of any appreciable value as sources of the anti-rachitic vitamins. Assays are expressed in terms of the International Units approved by the League of Nations. Fish liver oils are among the

### Value of Fish Liver Oils

richest sources of the vitamin ; cod liver oil, used for many years as an anti-rachitic agent, varies in its D content, depending on the season, the state and age of the fish and the particular fishing ground. Values range from 50 to 300 units per gm., but an average figure of 100 can be accepted.

The liver oils of other fish vary widely in their vitamin D content. Some contain none, many contain as much as is found in average cod liver oils, while others are much richer. Thus halibut liver oil contains from 800 to 4,000 units per gramme, swordfish liver oil up to 10,000 or 15,000, and certain fish of the tunny family yield a liver oil which varies from 30,000 to 80,000 units per gramme.

### Anti-Rachitic Potency of Common Foods in terms of Vitamin D content

| International Units per gm. |      |         | These values can be contrasted<br>with the following : |        |
|-----------------------------|------|---------|--------------------------------------------------------|--------|
|                             |      |         | International Units per gm.                            |        |
| Milk                        | .... | 0-0.1   | Crookes' Halibut                                       |        |
| Butter                      | .... | 0.4-4.0 | Liver Oil                                              | 2,500  |
| Cream                       | .... | 0.5     | „ Halycalcyne                                          | 8,000  |
| Egg yolk                    | .... | 1.5-5.0 | „ Super D Oil                                          | 50,000 |
| Calf liver                  | .... | 0       |                                                        |        |
| Olive oil                   | .... | 0       |                                                        |        |

*See also References on pages 40-42.*

## The Dental Field

A very important practical application of the results of animal experiments with vitamin D has been made in Sheffield, where investigations have been made to ascertain, firstly, whether the structure and arrangement of teeth in children can be influenced favourably by dietetic measures applied during the period of their development, and, if so, whether such teeth are less prone to develop caries, and secondly, whether the incidence and rate of progress of caries in teeth can be lessened by the adoption of similar dietetic measures. Evidence of a striking character has been obtained. In strictly comparable groups of children the progress of caries in permanent teeth was definitely retarded by the administration of vitamin D. In the words of the Report : “ The facts indeed seem to warrant the conclusion that the incidence and rate of progress of caries in teeth, either fully or nearly fully calcified, can be considerably retarded by the addition of fat-soluble vitamins to the normal diet.” A comparison of the various groups makes it highly probable that the potent factor in securing this retardation is vitamin D.

There are indications from other work that the results of the treatment of caries with vitamin D are greatly superior when calcium preparations are given at the same time.

It seems certain that some protection in the form of extra vitamin D is needed to keep teeth sound on the low calcium and phosphorus diets of modern times.

It must also be borne in mind that the formation of sound teeth in childhood is dependent on a regular and adequate supply of ascorbic acid (vitamin C). (*See page 33.*)

### In Allergy and Arthritis

Rappoport has found large doses of D (120,000 to 300,000 International Units daily) beneficial in 212 cases of hay fever and asthma. Dreyer and Reed found clinical improvement in 44 out of 67 cases of arthritis treated similarly.

# VITAMINS E

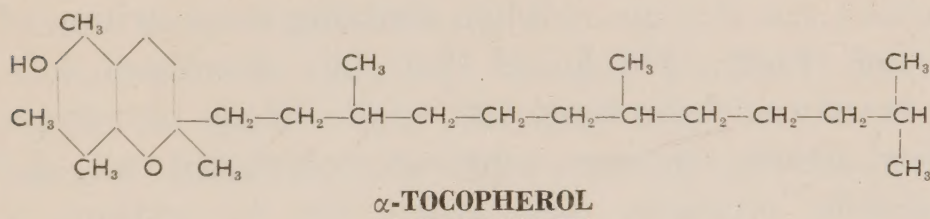
( $\alpha$ ,  $\beta$  and  $\gamma$ -Tocopherols)

## The Anti-Sterility Factor

These vitamins, for there are believed to be two or three closely related factors, play an important part in the reproductive cycle, probably, as recent work indicates, through the intermediary of the anterior lobe of the pituitary gland. Female animals, deprived of a sufficiency of these essential factors, show a characteristic type of secondary sterility. Pregnancy, which begins in a perfectly normal manner, is suddenly terminated by the death and resorption of the foetus. In the male a deficiency of E may cause premature degeneration of the spermatogenic tissues. The vitamins are found in green plant tissues, but the richest source is the oil extracted from wheat embryo. This oil, and concentrates prepared from it, have been used successfully in the treatment of certain forms of sterility in farm animals which have lately been suspected of E-deficiency conditions. In Denmark, Canada, and more recently in this country, similar treatment has also been applied, again with a good deal of success to certain forms of habitual abortion in women. In a series of twenty-eight women who had experienced two or more abortions, twenty-one treated with wheat germ oil produced healthy children.

The pure vitamins have recently been isolated as colourless, viscous oils. They are alcohols, having the composition  $C_{29}H_{48}O_2$ .

One of them,  $\alpha$ -tocopherol, has been found to possess the chemical structure



It has been synthesised recently, but artificially prepared material has not yet become available for clinical use. It seems likely that the related compounds  $\beta$  and  $\gamma$ -tocopherol have similar chemical constitutions.

# VITAMIN K

(Koagulations—vitamin)

## Fat-soluble Dietary Factor

This was discovered by Professor Dam, of Copenhagen, when studying the nutrition of young chicks. He found that they developed subcutaneous and intramuscular hæmorrhages on certain diets which, it was supposed, contained all the requisite vitamins, and there was in addition a marked anæmia. Superficially resembling scurvy the condition did not respond to additional ascorbic acid, but did to extracts prepared from certain green vegetables and liver.

The vitamin is one of the fat-soluble group, and chemical studies have nearly achieved its isolation. It appears to play an essential *rôle* in the formation of prothrombin, because the blood of affected animals shows greatly decreased clotting-time.

Studies to ascertain whether it plays any part in man are in the early stages.

As yet the application of vitamin K treatment in cases of hæmophilia has given negative results, but Professors Dam and Glavind have recently reported that vitamin K is of practical value in the treatment of cases of obstructive jaundice associated with reduced prothrombin-content of the blood. They suggest in their paper that the treatment with parenteral intro-

duction of vitamin K will completely substitute the old bile therapy.

### Vitamin K in Plants

Professors Dam and Glavind made a detailed study of the distribution of vitamin K in plants by a modification of the curative test method of Schonheyder (*Biochem. J.*, 1936, 30, 890 ; *Analyst*, 1936, 61, 567). The following values expressed in units of vitamin K per g. of dry material were obtained :

|                             |                       |
|-----------------------------|-----------------------|
| Green leaves :              | Seeds :               |
| Alfalfa .....200-400        | Soya bean .... 25     |
| Cabbage .....400            | Wheat Germ            |
| Spinach .....550            | less than .... 5      |
| Fruits : Strawberry .... 15 | Roots : Potatoes less |
| Tomato, ripe 50             | than ..... 10         |

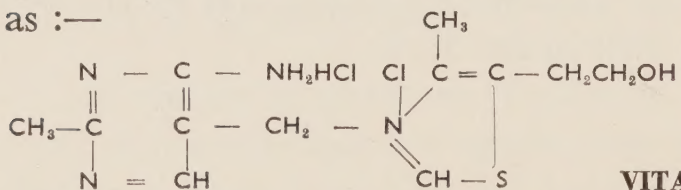
Leaves of the chestnut lost only a small portion, if any, of their vitamin K during the withering process, but etiolated leaves contained much less of the vitamin than the corresponding green leaves. In experiments with peas grown in the light and in the dark it was found that a large amount of vitamin was synthesised in the light, but little in the dark.

# VITAMIN B<sub>1</sub>

(Aneurin)

Anti-neuritic  
Factor

This factor is the anti-beri-beri or the anti-neuritic vitamin, the existence of which was suspected by Eijkmann nearly forty years ago when his classic researches on the relation between experimental polyneuritis in fowls and human beri-beri were in progress. It is a fitting sequel to this remarkable series of pioneer investigations that after many years the vitamin was ultimately isolated in the same laboratory by two of Eijkmann's successors in the Medical Service of the Dutch East Indies, Dr. Jansen and Dr. Donath. From large quantities of rice polishings they isolated a few milligrams of a beautifully crystalline hydrochloride of an organic base which possessed all the physiological properties of the substance they were seeking. A microphotograph of the crystals is shown in *Fig. 2, page 3*. Its formula proved to be  $C_{12}H_{18}ON_4Cl_2S$ , and by a series of brilliant researches by organic chemists its constitution has been revealed as :—



VITAMIN B<sub>1</sub> (Aneurin)

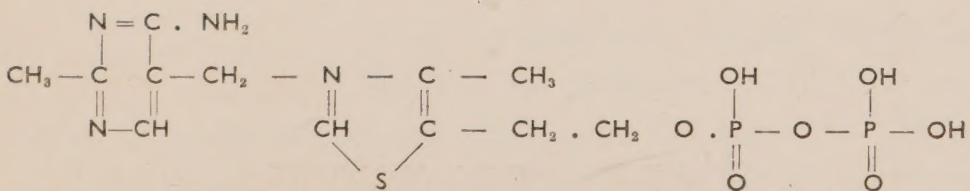
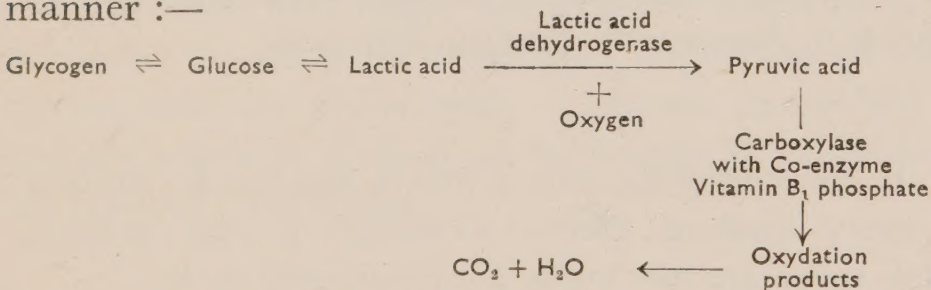
The synthesis was later accomplished in the U.S.A. by Williams and Cline, and it is now possible to produce the laboratory-prepared vitamin in large

amounts. Its physiological activity is identical with that of the natural product. From extracts of natural products containing the vitamin the active principle can be separated by adsorption on solids such as fuller's earth. Such preparations, known generally as "activated earths," are often used as convenient forms in which to administer vitamin B<sub>1</sub> by the mouth. For intravenous or subcutaneous injection solutions of the hydrochloride of the vitamin itself are employed.

## Physiological Role

It has been discovered that aneurin plays a direct part in one phase of carbohydrate metabolism. In the form of a compound with pyrophosphoric acid it acts as the co-enzyme to the enzyme which breaks down pyruvic acid, one of the intermediate products between glucose and carbon dioxide.

This can be shown schematically in the following manner :—



**CO-ENZYME OF PYRUVATE CARBOXYLASE**  
(Aneurin pyrophosphate)

See also References on pages 40-42.

A deficiency of vitamin B<sub>1</sub> causes the efficiency of the pyruvate-metabolising mechanism to be lowered, with the result that the amount of pyruvate in the blood tends to rise. This abnormality can be detected either by estimating the amount of pyruvic acid by direct combination with 2:4-dinitrophenylhydrazine, or, less accurately, by determining the amount of substance in the blood which will combine with bisulphites.

The amount of pyruvic acid rises sharply in “florid” beri-beri, as seen in the Orient, and the analytical data are useful in diagnosis and treatment. There is some evidence that this excessive amount of pyruvates is responsible for some of the symptoms.

Vitamin B<sub>1</sub> deficiency of this severity is seldom seen in Western Europe, but milder forms, usually very difficult to detect, are certainly common.

In the first place, this is due to the low B<sub>1</sub> content of many modern diets. Contrary to the general belief, there are not many foodstuffs rich in B<sub>1</sub>.

## Human Requirements

The close relation of B<sub>1</sub> to metabolism has led to the discovery of a simple equation by which the mini-

imum requirements of man can be ascertained from the body weight and the calorific value of the diet. Cowgill's formula is :—

$$\text{Vitamin intake (in International Units)} = \\ \text{Calorific intake} \times \text{Wt. (Kg.)} \times 0.0284.$$

This formula has been found to hold in the examination of a very large number of cases.\*

The minimum requirement of an adult taking a daily diet of about 3,500 calories can be taken, therefore, at about 550 International Units. Allowing a margin for safety, this may be increased to 700. Many modern diets supply only about 350. The beri-beri "danger-line" appears to be about 200.

There is, however, considerable danger of vitamin B<sub>1</sub> deficiency arising when patients are on restricted diets, such as in ulcer treatment, or where individuals cut their own food intake down, either deliberately or by heavy smoking or drinking. Joliffe has recently shown that the polyneuritis of chronic alcoholism is usually traceable to shortage of vitamin B<sub>1</sub> consequent on reduced food intake.

### In Childhood

The weight-food intake formula applies to children. There is no need to make a special allowance for growth. It is well, however, to err on the liberal side, for it is certain

\* "The Vitamin B Requirement of Man," G. R. Cowgill, New Haven, 1934.

that a large excess of the vitamin is without any ill-effects.

Daily intakes of 300–500 International Units will certainly cover children's requirements.

**In Pregnancy**

This condition demands a much increased intake. Daily doses as high as 1,000 International Units or even higher are advised.

## Vitamin B<sub>1</sub> content of Foods

Expressed as International Units per gm.

|                                  |         |                               |           |
|----------------------------------|---------|-------------------------------|-----------|
| Meats (other than<br>pork) ..... | 0.2–1.9 | Vegetables .....              | 0.3–1.6   |
| Roast pork .....                 | 3.2     | Fruits .....                  | about 0.4 |
| Ham .....                        | 2.2     | Nuts .....                    | 0.5–2     |
| Fish .....                       | 0.3–0.6 | Whole wheat .....             | 2.3–3.4   |
| Milk .....                       | 0.2     | Wheat germ .....              | 8.5–18.7  |
| Cheese .....                     | 0.3     | Oatmeal .....                 | 3         |
| Egg yolk .....                   | 1.4     | Dried brewer's<br>yeast ..... | 6–23      |

# VITAMIN B<sub>2</sub>

(Riboflavin)

## Tissue Oxidation Factor

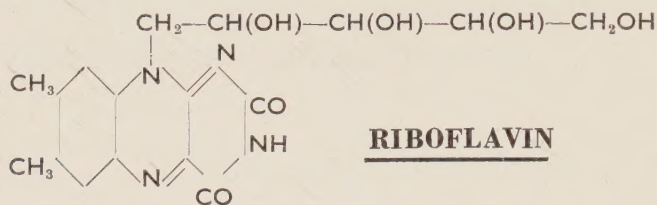
When studies of the human disease pellagra and of a related condition observed in certain laboratory animals revealed that the disorders arose as a result of deprivation of a water soluble vitamin, often associated with B<sub>1</sub> but clearly differentiated from that substance; this new factor was labelled B<sub>2</sub>. Later work demonstrated that at least two substances were concerned. One of these has been isolated and identified. To it has stuck the original label B<sub>2</sub>, although it is often referred to by its more descriptive name riboflavin.

It was for a time called lactoflavin, but that name is now superseded by one which gives a better clue to its chemical structure.

It is a yellow pigment found in certain foods, particularly in the watery fraction of milk, in extracts from liver, and in yeast. It is responsible to a large extent for the peculiar greenish yellow colour of whey—hence its name. When isolated it is a golden brown crystalline

*See also References on pages 40-42.*

solid (*see Fig. 4, page 2*) of composition C<sub>17</sub>H<sub>20</sub>N<sub>4</sub>O<sub>6</sub> and its constitution has been determined as :—



6.7. dimethyl-9-ribityl-isoalloxazin

Synthesis has confirmed this suggested constitution.

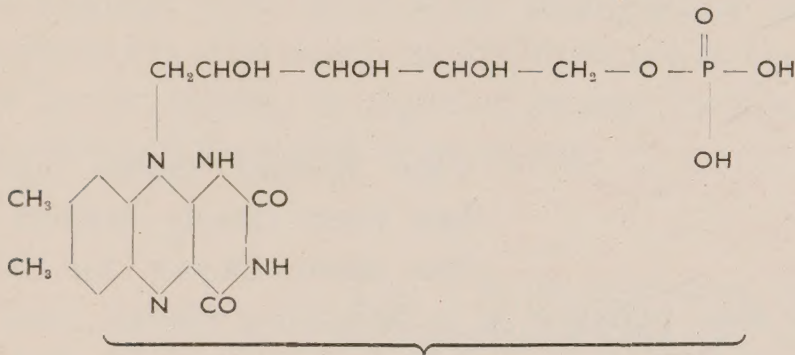
## Physiological Rôle

One of the most important enzymes concerned with oxidation in the body tissues—indeed, in all tissues, for it is found universally in nature—is the so-called “yellow respiration-ferment” of Warburg.

This enzyme has been isolated by the brilliant German biochemist as a golden yellow powder. It proves to be a conjugated protein. The prosthetic group attached to the protein, which confers on the whole complex peculiar and specific properties, is essentially the unit riboflavin.

It is, however, also in combination with phosphoric acid, as are so many of the agents taking part in metabolic changes in the organisms. The “yellow-

ferment" of Warburg can, therefore, be represented as follows :—



**PROTEIN YELLOW FERMENT OF WARBURG**

Riboflavin is therefore indispensable to the normal functioning of the oxidising system of all cells. It is not known what part it actually plays in the tissues, nor is there as yet any clear indication of the defects which are caused by its deficiency in man. All that is known is that it cannot be synthesised by the organism and that it is essential to cellular respiration. There are indications that a deficiency of Riboflavin may be associated with one form of cataract.

**Riboflavin content of Foods**

*N.B.*—There is as yet no approved International Unit. Estimations are, therefore, expressed in actual amounts of the vitamins :—

|                        | Riboflavin<br>mgm. per 100 gm. |                 | Riboflavin<br>mgm. per 100 gm. |
|------------------------|--------------------------------|-----------------|--------------------------------|
| Cows' milk .....       | 0.1                            | Cod .....       | 0.05                           |
| Hens' eggs, yolk ..... | 0.5-0.6                        | Ox liver .....  | 0.1-2.4                        |
| „ „ white .....        | 0.4-0.5                        | Ox kidney ..... | 0.8-1.6                        |
|                        |                                | Yeast .....     | 1.8-3.6                        |

*See also References on pages 40-42.*

# P. P FACTOR

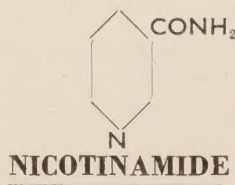
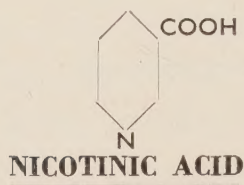
(Nicotinic Acid)

## The Anti-Pellagra Vitamin

This dietary factor has at last been clearly defined. It has been known for fifteen years that pellagra is a deficiency disease, and for most of that time it has been suspected that the deficiency responsible was in respect to a member of the vitamin group.

At one time it was thought that this factor might be riboflavin, but tests on pellagrins proved negative. Provisionally the factor was given the label P.P vitamin, meaning pellagra-preventive.

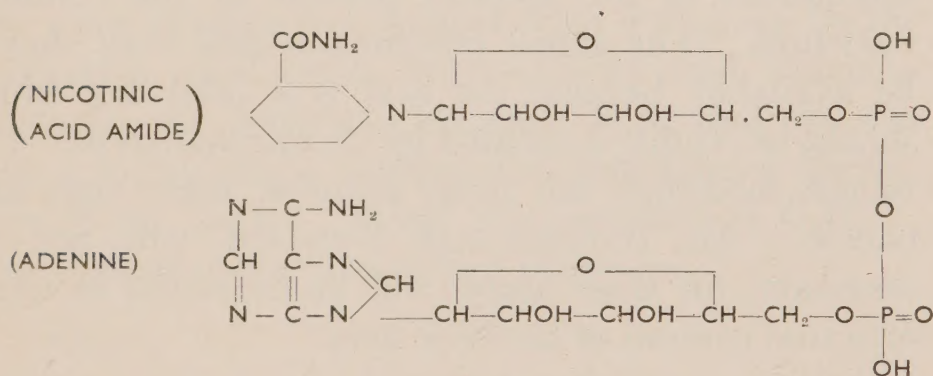
Until recently, however, there was some uncertainty whether other dietary defects, toxic substances in spoilt grain, protein of low biological value, etc., might not be in part also concerned. There is no longer any doubt. The work of Elvehjem and his colleagues at Madison, Wisconsin, showed clearly that pellagra-like conditions produced in certain animals by deficient diets could be cured by administering nicotinic acid or its amide.



The application of this knowledge to the treatment of human pellagra has proved a brilliant success. Cases respond with remarkable promptitude to the administration of amounts ranging from 100 to 500 mg. given by the mouth, or repeated dosage by injection of quantities of the order of 10–20 mg.

**Its function in the Body**

This is as yet unknown, but it is significant that the amide of nicotinic acid is part of the molecule of the co-enzyme co-zymase, which plays an important part in carbohydrate breakdown.



**CO-ZYMASE**

**Pellagra in England**

Pellagra in its well-known form is endemic among maize-eating populations, and is often regarded as unknown in Western Europe. Actually, however, a number of clear-cut cases, showing the typical “sun-

*See also References on pages 40–42.*

burn " area dermatitis, sore tongue, gastro-intestinal disturbances and mental disorders have recently been described. In most cases they were what have been called "secondary pellagra," that is, deficiency conditions arising from the individual having been a long time on a very restricted diet, *e.g.*, chronic ulcer cases, food cranks, etc.

### Nicotinic Acid content of Foods

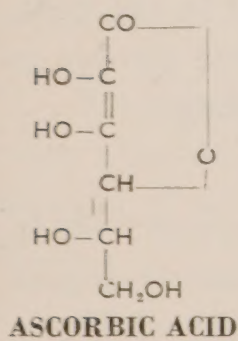
There is, at present, no recognised International Standard for nicotinic acid, nor are there available any estimations of the amount present in the common foodstuffs. The latter information will very shortly be available, because the acid is a substance which should be readily estimated by chemical analysis. The richest foodstuffs are liver, kidneys, milk, eggs and cheese. An International Standard will not be necessary, for these assays will be expressed in terms of actual content of nicotinic acid.

# VITAMIN C

(Ascorbic Acid)

Anti-scorbutic  
Factor

The long recognised value of fresh fruit and vegetables in preventing the onset of scurvy has for the past twenty years been correlated with the presence in these foodstuffs of a substance of the vitamin class. It was sometimes known as the anti-scorbutic vitamin C, but the name ascorbic acid has been given to it since its isolation and identification. The pure vitamin was isolated from fruit juice by the Hungarian biochemist Szent-György and independently by the American scientists King and Waugh. It is a feebly acidic substance closely related chemically to the sugars. It has the composition  $C_6H_8O_6$  and its constitution is as shown below :—



It has recently been synthesised and the laboratory prepared compound is now available. The crystalline form of the acid is shown in *Fig. 5, page 2*. Expeditions which formerly had to depend on preserved and concentrated fruit juices for protection against scurvy can now rely on convenient tablets of the pure acid.

*See also References on pages 40-42.*

The International Unit for ascorbic acid assays is based on the activity of 0.05 mg. of the pure acid.

### Forms of Scurvy

Scurvy in adults is rarely encountered at the present time. Severe outbreaks were observed in Murmansk in 1919, and in the famine areas of Russia in 1922, but in Western Europe and America it is seldom seen.

The other form of scurvy, namely, infantile scurvy, is also fast disappearing owing to the general recognition of the value of fruit juice in supplementing the possible deficiency of a milk diet. It was some time before it was generally recognised that cows' milk is rather a poor source of vitamin C, and a good deal was written about the dangers of lowering the anti-scorbutic value of this foodstuff by boiling, pasteurising or sterilising. Actually, although it is probable that the heating of milk decreases the amount of vitamin C present in cows' milk, the amount present in the fresh product is so small as to make it advisable always to supplement with fruit juice for infant feeding.

### Pre-scorbutic Conditions

An important discovery, made originally in Scandinavia, is that individuals, particularly children, may show an increased fragility of the capillaries in the early spring. This condition is very common in northern climates where fresh fruit and vegetables are scarce during the winter. In one district of Sweden one of every five "healthy" children showed this

condition at the end of the long winter. It is to-day recognised as an early stage in the development of scurvy.

### Ascorbic Acid and Teeth

Loosened teeth and swollen bleeding gums are characteristic symptoms of scurvy. They are seldom seen in Western Europe to-day. On the other hand, there is evidence that chronic, even if slight, deprivation of vitamin C adversely affects dentition. An adequate supply of vitamin C is an essential for the development and maintenance of sound teeth.

### Vitamin C in Febrile Conditions

There is evidence that depletion of the vitamin C in the body tissues occurs more rapidly in febrile conditions than normally. There are, therefore, indications for increased intake in such cases.

## Human Requirements

To prevent the appearance of symptoms associated with the pre-scorbutic condition children should be assured of at least 50 mg. (1,000 International Units) daily.

There can be no objections to larger doses (100 mg.) for growing children if, between 5 and 15 years of age, vitamin lack is suspected. Adults require at least 50 mg. daily. In pregnancy the demand is greater and doses as large as 150 mg. are indicated.

*See also References on pages 40-42.*

## The Detection of Vitamin C Insufficiency

The reduction of the coloured dyestuff, 2-6-dichloro-phenol-indophenol, to a colourless substance by ascorbic acid is widely used as a clinical test for determining vitamin C deficiency or saturation. It is important to remember that vitamin C, like other water-soluble vitamins, is excreted in the urine, and that this is responsible for a daily depletion of the stores in the body. Titration of the urine with a standard solution of the indicator mentioned gives a reasonably accurate method of determining the amount of ascorbic acid excreted in 24 hours. The reaction must be carried out at an acidity represented by pH 2 or 3, in order to eliminate the possibility of interference by other reducing substances.

When an adult is receiving ample vitamin C in the diet the daily excretion by way of the urine appears to be of the order of 20–30 mg. When the amount is less than 15 mg., it is an indication of insufficiency. The “saturation” test devised by Harris and Ray is of great value in determining whether a patient is in a depleted condition or not. It is carried out by ascertaining how much ascorbic acid appears in the urine during the three or four days after administering a single dose of vitamin.

An appropriate dose is 70 mg. per kilo of body weight. It may be necessary, if the subject is in a state of serious depletion, to repeat the dosage on two or even more successive days until evidence of a

re-saturation of the tissues is obtained. The details of this test will be found in the papers by Harris and his colleagues given in the list of references. (*See pages 40-42.*)

#### Intradermal Test

A very much simpler test depending on the time taken for a small quantity of a solution of dichloro-phenol-indophenol injected under the skin to lose its colour (intradermal test) is gaining considerable popularity as the results seem to be in good agreement with those given by more accurate, but more time-consuming, methods of estimating the vitamin C content of the blood and tissues. (*See page 42 for references to papers on intradermal test.*)

#### Capillary Fragility Test

The “capillary resistance” test, devised by Göthlin for detecting “sub-scurvy,” appears to be fairly reliable when infants and young children are being investigated, but is untrustworthy when applied to adults. It depends on counting the number of petechiae formed in a certain area of the skin of the forearm after raising the pressure in the limb a definite amount by a tourniquet or after applying a certain negative pressure to the particular surface of the area of skin itself.

### Vitamin C content of Foods

Fresh fruits, vegetables and fruit juices are the best natural sources of the vitamin. Cereals do not

*See also References on pages 40-42.*

## VITAMIN C—continued.

contain it, but appreciable amounts are found during germination. Germinated seeds have on more than one occasion been successfully employed as anti-scorbutics in emergency. The amounts present in important foods are given below.

|                     | Mgm. per 100 gm. |               | Mgm. per 100 gm. |
|---------------------|------------------|---------------|------------------|
| Lemon juice .....   | 25-70            | Lettuce ..... | 3-8              |
| Orange juice .....  | 20-60            | Onions .....  | 2-10             |
| Black currant ..... | 130-220          | Cabbage ..... | 20-40            |
| Red currant .....   | 40-50            | Spinach ..... | 30-70            |
| Marmalade .....     | 6-14             | Milk .....    | 1-2              |
| Tomatoes .....      | 12-25            |               |                  |

## VITAMIN P

This label was attached to a factor in lemon juice which Rusznyak and Szent-György studied. They found the juice to be more effective than ascorbic acid in the treatment of certain types of nutritive disorder characterised by increased permeability of the capillaries. The supplementary factor appeared to be identical with or associated with one of the yellow water-soluble pigments of the flavine type.

Their experiments indicated that the natural pigment, hesperidine, might be identical with the P-factor, but the position is not quite clear yet. Other workers have denied that such a factor exists. There is as yet insufficient evidence to state whether lemon juice is nutritively superior to the amount of ascorbic acid which it contains, although Elmby and Warburg have recently stated that they have observed that some human cases respond as if this were true.

*See also References on pages 40-42.*

# THE VITAMINS

## INTERNATIONAL STANDARDS

AND

## METHODS OF ESTIMATION

|                      |                                                                                                                                                                                                                                                                                                               | International<br>Units | International<br>Units per gramme<br>of Pure Vitamin |
|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------------------------------------------|
| <b>A</b>             | <b>International Standard.</b><br>Pure $\beta$ -carotene. 0.6 gamma =<br><i>Estimated by growth test on young rats against<br/>International Standard and by ultra-violet<br/>spectrophotometer, pure vitamin A being<br/>defined as having—</i><br>$E \frac{1\%}{1 \text{ cm}}$ at $\lambda$ 3280 Å of 1600. | I                      | 2,560,000                                            |
| <b>D<sub>2</sub></b> | <b>International Standard.</b><br>Pure calciferol. 0.25 gamma =<br><i>Estimated by the cure of rickets in young rats<br/>fed on a rachitogenic diet against pure calci-<br/>ferol.</i>                                                                                                                        | I                      | 40,000,000                                           |
| <b>D<sub>3</sub></b> | <b>Natural.</b><br><i>Distinguished from pure calciferol by the<br/>ratio of its action on young rats and on young<br/>chicks compared to the action of calciferol.</i>                                                                                                                                       | —                      | Probably<br>in man<br>40,000,000                     |
| <b>E</b>             | <b>No International Standard</b> is available<br><i>No satisfactory method of estimating this<br/>vitamin has yet been evolved.</i>                                                                                                                                                                           | —                      | —                                                    |
| <b>B<sub>1</sub></b> | <b>International Standard.</b><br>Standard adsorbate of this vitamin,<br>10 mg. of which =<br><i>Estimated by growth test on young rats, and<br/>more recently by curative action on brady-<br/>cardia by the method of Birch and Harris,<br/>against the International Standard.</i>                         | I                      | —                                                    |
| <b>B<sub>2</sub></b> | <b>International Standard.</b><br>Pure lactoflavine is available<br><i>The Sherman-Borquin Unit often quoted is<br/>based on a method not specific for lactoflavine.</i>                                                                                                                                      | Not fixed              | —                                                    |
| <b>C</b>             | <b>International Standard</b><br>Pure ascorbic acid is available as<br>standard, and 0.5 mg. =<br><i>Estimated by the bleaching of phenol-indo-<br/>phenols (other substances may give this reaction<br/>also) and by biological test on guinea-pigs<br/>against the pure substance.</i>                      | I                      | 20,000                                               |

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|                       |                                |      |           |
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|                             |                           |      |          |
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## GENERAL LITERATURE

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Vol. 5. Relation of Nutrition to Health, Agriculture and  
Economic Policy..... 1937 3s.

## TABLE OF VITAMIN CONTENT OF FOODSTUFFS

Published by nutrition abstracts and obtainable, price 2s. 6d., from Imperial Bureau of  
Nutrition, Rowett Institute, Bucksburn, Aberdeen.

# Crookes' Vitamin Preparations

(Standardised)

A and D In  
HIGH POTENCY

52,000 A<sub>1</sub> } International Units  
2,500 D<sub>3</sub> } per gramme.

\* Crookes' Halibut Liver Oil. The original and only guaranteed halibut liver oil available is issued as drops and in 3 minim capsules for easy administration to infants or adults.

A and D with  
CALCIUM

40,000 A<sub>1</sub> } International Units  
8,000 D<sub>3</sub> } per gramme.

\* Halycalcyne (Crookes' Halibut Oil with Calcium Phosphate) is for the prevention of dental decay, and for the treatment of calcium deficiency diseases.

A and D In  
EMULSION

1,780 A<sub>1</sub> } International Units  
61 D<sub>3</sub> } per gramme.

\* Halidexol (the emulsion form of Crookes' Halibut Oil) is equivalent in vitamin A value to its own volume of pure cod liver oil with adequate vitamin D. Ideal for adding to the baby's feed. One third teaspoonful is equal to one drop of halibut liver oil.

\* A guarantee of vitamin content  
is affixed to every package issued.

For table of vitamin content per  
dose, see page 48.

Prices and packings see pages 51-52.

## CROOKES' VITAMIN PREPARATIONS—*continued.*

(Standardised)

**A and D in  
MALT**

1,070 A<sub>1</sub> } International Units  
105 D<sub>3</sub> } per gramme.

\*Halimalt (Crookes' Halibut Oil with malt extract) embraces malt extract made from the finest Scotch winter-malted barley, and presents the highest nutritional advantages.

**A, C and D with  
GLUCOSE**

670 A<sub>1</sub> } International Units  
51 D<sub>3</sub> } per gramme.

\*Halycitrol (Crookes' Halibut Oil with orange juice and glucose) enables halibut oil to be taken with the greatest ease, particularly during the summer.

**D with  
CALCIUM**

250 D<sub>3</sub> } International Units  
per teaspoonful.

Collosol Calcium with vitamin D presents approximately 1 per cent. of a colloidal calcium salt of fatty acids with 250 International Units of vitamin D for the oral treatment of rickets and other important indications where administration of vitamin D is essential.

\* A guarantee of vitamin content is affixed to every package issued.

For table of vitamin content per dose, see page 48.

Prices and packings see pages 51-52.

## CROOKES' VITAMIN PREPARATIONS—*continued.*

(Standardised)

|                                   |                                                            |                                                    |
|-----------------------------------|------------------------------------------------------------|----------------------------------------------------|
| <b>MASSIVE D</b><br><b>with A</b> | <b>52,000 D<sub>3</sub></b><br><b>65,700 A<sub>1</sub></b> | <b>} International Units</b><br><b>per gramme.</b> |
|-----------------------------------|------------------------------------------------------------|----------------------------------------------------|

Crookes' standardised Super-D Oil (natural) is for the administration of massive doses of vitamins D and A.

Of service in the treatment of such conditions as rickets where a large amount of vitamin D is essential and indicated to effect a cure, also in hay fever, asthma and arthritis.

Is issued in two forms, viz., as drops and capsules.

| Content.          | International Units. |        |
|-------------------|----------------------|--------|
|                   | D                    | A      |
| Each drop.....    | 1,350                | 1,700  |
| Each capsule..... | 8,000                | 10,000 |

|                                      |                                                        |                                                    |
|--------------------------------------|--------------------------------------------------------|----------------------------------------------------|
| <b>A and D in</b><br><b>EMULSION</b> | <b>2,000 A<sub>1</sub></b><br><b>200 D<sub>3</sub></b> | <b>} International Units</b><br><b>per drachm.</b> |
|--------------------------------------|--------------------------------------------------------|----------------------------------------------------|

Crookes' Emulsion—physiologically standardised—is a scientifically prepared emulsion containing 50% of the purest cod liver oil. Miscible with three or four times its bulk of water, milk or wine.

Issued also with Collosol Calcium, Lecithin, Iodine and Yeast.

|                                                              |                                                        |                                                         |
|--------------------------------------------------------------|--------------------------------------------------------|---------------------------------------------------------|
| <b>A and D with MALT, EGGS,</b><br><b>MILK and CHOCOLATE</b> | <b>1,400 A<sub>1</sub></b><br><b>130 D<sub>3</sub></b> | <b>} International Units</b><br><b>per teaspoonful.</b> |
|--------------------------------------------------------------|--------------------------------------------------------|---------------------------------------------------------|

Halcova embraces vitamins A and D in the form of pure standardised halibut liver oil, and this preparation when mixed in the proportions of a teaspoonful to a cup of hot milk makes an ideal beverage.

*For table showing vitamin content per dose, see page 48.*

*Prices and packings see pages 51-52.*

## CROOKES' VITAMIN PREPARATIONS—continued.

(Standardised)

**B<sub>1</sub> and D in  
GLUCOSE**

300 B<sub>1</sub> } International Units  
300 D<sub>3</sub> } per ounce

Crookes' Glucose B-D is designed to provide a pleasant means of absorbing an easily assimilable and powerfully energising food, amplified with the two vitamins least plentiful in modern diet, and which vitamins are necessary not only to repair physical damage, but to set up a physical defence against possible recurrence of such damage.

**B<sub>1</sub> CAPSULES  
(oral)**

300 { International Units  
per capsule

Used for the administration of massive dosage of B<sub>1</sub> vitamin in the treatment of anorexia, debility and cardiac affections. Vitamin B<sub>1</sub> is closely connected with the process of cell metabolism. In its absence the oxidation of glucose to produce energy fails to proceed beyond a certain point, and the result is that valuable energy is lost and nerve degeneration may commence. *For B<sub>1</sub> injection see page 50.*

**D and C  
in MALT**

250 D<sub>3</sub> { International Units  
per drachm.

Crookes' F.C.V.D. (Collosol Ferro-Cuprum with vitamin D and natural orange juice). A tonic food which does not constipate, but which enables the administration of activated iron in the treatment of anæmia without digestive disturbance or staining of teeth. Its vitamin D content plays a highly important part in promoting calcium absorption.

*For table showing vitamin content per dose, see page 48.*

*(Standardised)*

|                                                      |                      |                                  |                        |
|------------------------------------------------------|----------------------|----------------------------------|------------------------|
| <b>B<sub>1</sub> and B<sub>2</sub><br/>in KAOLIN</b> | <b>B<sub>1</sub></b> | <b>70 International Units</b>    | } <b>Per<br/>ounce</b> |
|                                                      | <b>B<sub>2</sub></b> | <b>25 Sherman-Bourquin Units</b> |                        |

Collosol Lacto-Kaolin with Vitamin B is designed to give the most beneficial effect in all disturbed conditions of the intestinal tract. (1) The Collosol Kaolin as an adsorptive in intestinal toxæmia. (2) The Lactose for changing intestinal flora from the coliform type to the lactic acid bacillus type. (3) The vitamin B to encourage a healthy condition of the intestine and normal peristalsis.

|                                                      |                      |                                   |                                      |
|------------------------------------------------------|----------------------|-----------------------------------|--------------------------------------|
| <b>B<sub>1</sub> and B<sub>2</sub><br/>with IRON</b> | <b>B<sub>1</sub></b> | <b>9·1 International Units</b>    | } <b>Per<br/>5-min.<br/>capsule.</b> |
|                                                      | <b>B<sub>2</sub></b> | <b>3·2 Sherman-Bourquin Units</b> |                                      |

Ferrofax (Ferrous iron and vitamin B) is specially adapted for the treatment of nutritional anæmia.

A combination of yeast and ferrous iron was found to give the best results of many mixtures tested.

Ferrofax, based upon this finding, but with vitamin B concentrate as a substitute for the yeast, is pleasant and easy to take, particularly for children.

### **E—WHEAT GERM**

**Collosol Brand Wheat Germ Oil**  
**The anti-sterility vitamin.**

Collosol Brand Wheat Germ Oil. The deficiency of vitamin E affects both sexes. Available in 3 minim capsules (each containing 200 milligrams).

*See page 50 for vitamin preparations for inunction and injection.*

*Prices and packings see pages 51-52.*

# VITAMIN CONTENT OF CROOKES' PREPARATIONS

In International Units per dose

|                             | Per Dose    | Oil Soluble Vitamins |                              |                           | Water Soluble Vitamins |                |       |
|-----------------------------|-------------|----------------------|------------------------------|---------------------------|------------------------|----------------|-------|
|                             |             | A                    | D <sub>2</sub><br>Calciferol | D <sub>3</sub><br>Natural | B <sub>1</sub>         | B <sub>2</sub> | C mg. |
| Halibut Liver Oil .....     | 3 Drops     | 4,600                | —                            | 220                       | —                      | —              | —     |
| “ “ .....                   | Capsule     | 8,800                | —                            | 485                       | —                      | —              | —     |
| Halycalcyne .....           | “           | 5,330                | —                            | 1,063                     | —                      | —              | —     |
| Halidexol .....             | Teaspoonful | 6,200                | —                            | 220                       | —                      | —              | —     |
| Halimalt .....              | “           | 4,300                | —                            | 420                       | + +                    | —              | 0.25  |
| Halycitrol .....            | “           | 2,600                | —                            | 200                       | —                      | —              | 2     |
| Calcium Vitamin D Oral....  | “           | —                    | —                            | 250                       | —                      | —              | —     |
| Super-D Oil .....           | 3 Drops     | 6,050                | —                            | 4,800                     | —                      | —              | —     |
| “ “ .....                   | Capsule     | 11,000               | —                            | 9,000                     | —                      | —              | —     |
| Glucose B-D .....           | Teaspoonful | —                    | —                            | 75                        | 75                     | —              | —     |
| Lacto-Kaolin with Vitamin B | “           | —                    | —                            | —                         | 23                     | + +            | —     |
| Ferrox .....                | 5 Minims    | —                    | —                            | —                         | 9.1                    | +              | —     |
| F.C.V.D. ....               | Teaspoonful | —                    | 250                          | —                         | + +                    | —              | 0.5   |

|                                       |             |       |       |      |       |   |
|---------------------------------------|-------------|-------|-------|------|-------|---|
| Wheat Germ Oil .....                  | Capsule     | —     | —     | —E + | —     | — |
| Crookes' Emulsion.....                | Teaspoonful | 2,000 | —     | 200  | —     | — |
| Halcova .....                         | "           | 1,400 | —     | 130  | +     | — |
| Calcium Vitamin D injection           | c.c.        | —     | 5,000 | —    | —     | — |
| Vitamin B <sub>1</sub> injection..... | "           | —     | —     | —    | 1,000 | — |
| " Oral .....                          | Capsule     | —     | —     | —    | 300   | — |
| Collotone.....                        | Teaspoonful | —     | —     | —    | +     | + |

### VARIOUS EQUIVALENTS

|                    |                  |           |   |       |     |                           |
|--------------------|------------------|-----------|---|-------|-----|---------------------------|
| Butter .....       | Per lb. (Winter) | 11,000    | — | 200   | —   | —                         |
|                    | (Summer)         | 23,500    | — | 1,650 | —   | —                         |
| Orange Juice ..... | Per ounce        | —         | — | —     | +   | 6.27                      |
| Eggs .....         | Average          | 300       | — | 15-50 | 14  | —                         |
| Cabbage .....      | Ounce            | 252       | — | —     | —   | —                         |
| Carrots .....      | "                | 532       | — | —     | —   | —                         |
| Cream .....        | "                | 900-1,500 | — | 0-30  | 3.6 | —<br>(only when<br>fresh) |
| Milk .....         | "                | 90-150    | — | 0-3   | 6   | 0.6                       |
| Cabbage .....      | Per lb.          | 4,000     | — | —     | 400 | 170                       |

# Vitamin Preparations

## for Inunction and Injection

A as  
OINTMENT

500 A<sub>1</sub> { International Units  
per gramme.

Collosol Brand Halibut Liver Oil Ointment is standardised to contain 500 International Units of vitamin A per gramme. It is soothing, antiseptic, anti-pruritic and imparts the direct regenerative or "healing" effect of vitamin A upon the skin cells. Its range of "indications" is wide and comprehensive and includes those minor skin troubles commonly met with in general practice.

D with  
CALCIUM

5,000 D<sub>3</sub> { International Units  
per c.c.

Collosol Calcium with Vitamin D presents Ca 1-2,000 with vitamin D in sterile solution, specially prepared for subcutaneous injection.

B<sub>1</sub> for  
Injection

1,000 B<sub>1</sub> { International Units  
per c.c.

Collosol Vitamin B<sub>1</sub> is for use in cases where this vitamin is not properly absorbed by the oral route. Specific in vitamin B deficiency, in cardiac affections, neuritis and polyneuritis.

*Prices and packings see pages 51-52.*

## Price List

## of Crookes' Vitamin Preparations

| See<br>page |                                                                               | Size.              | Each. |
|-------------|-------------------------------------------------------------------------------|--------------------|-------|
|             | <b>B<sub>1</sub> VITAMIN.</b> See Vitamin B <sub>1</sub> on page 52           |                    |       |
| 50          | <b>CALCIUM c VITAMIN D</b>                                                    |                    |       |
|             | <b>Injection</b>                                                              |                    |       |
|             | (Ca. 1-2000 : vitamin D, 5000 Int'l. units per c.c.) Ampoules (Box of 6)..... | $\frac{1}{2}$ c.c. | 3/9   |
|             | " " .....                                                                     | 1 c.c.             | 5/-   |
|             | " " .....                                                                     | 2 c.c.             | 8/6   |
| 44          | <b>Oral</b>                                                                   |                    |       |
|             | (Ca. 1-2000 : vitamin D, 250 Int'l. units per fl. drachm)                     |                    |       |
|             | Bottles .....                                                                 | 4 oz.              | 4/6   |
|             | " .....                                                                       | 10 oz.             | 9/6   |
|             | " .....                                                                       | 20 oz.             | 17/-  |
|             | " .....                                                                       | 40 oz.             | 32/6  |
|             | " .....                                                                       | 80 oz.             | 63/-  |
|             | <b>Capsules</b> (each=1 teaspoonful or fl. drachm Oral) Vials .....           | 25                 | 3/6   |
| 45          | <b>CROOKES' EMULSION (50% Cod Liver Oil)</b>                                  |                    |       |
|             | Bottles .....                                                                 | 6 oz.              | 2/-   |
|             | " .....                                                                       | 12 oz.             | 3/6   |
|             | " .....                                                                       | 40 oz.             | 10/-  |
|             | " .....                                                                       | 80 oz.             | 18/6  |
|             | " " with Collosol Calcium.....                                                | 6 oz.              | 2/6   |
|             | " " " " " Lecithin } .....                                                    | 12 oz.             | 4/-   |
|             | " " " " " and Col. Iodine } .....                                             | 40 oz.             | 11/-  |
|             | " " " Yeast .....                                                             | 80 oz.             | 21/-  |
| 46          | <b>'F.C.V.D.' (Collosol Ferro Cuprum c Vitamin D in Malt Extract)</b>         |                    |       |
|             | Bottles .....                                                                 | 8 oz.              | 4/-   |
|             | " .....                                                                       | 40 oz.             | 17/6  |
|             | " .....                                                                       | 80 oz.             | 32/6  |
| 47          | <b>FERROFAX (Vitamin B complex with Iron)</b>                                 |                    |       |
|             | Capsules ..... Vials (Child's) .....                                          | 25                 | 2/6   |
|             | " " (Adult) .....                                                             | 100                | 8/6   |
|             | Powder Bottles .....                                                          | 50                 | 5/6   |
|             | " .....                                                                       | 8 oz.              | 4/-   |
| 46          | <b>GLUCOSE B-D</b>                                                            |                    |       |
|             | Tins .....                                                                    | 16 oz.             | 2/6   |
| 45          | <b>HALCOVA (Vitamins A and D with Malt, Eggs, Milk, Chocolate)</b> .....      | Tins               | 1/6   |

PRICE LIST—*continued.*

| See<br>page |                                                                              |                                     | Size     | Each |
|-------------|------------------------------------------------------------------------------|-------------------------------------|----------|------|
| 43          | <b>HALIBUT LIVER OIL (Crookes') Standardised</b>                             |                                     |          |      |
|             | The Oil                                                                      | Vials .....                         | 5 c.c.   | 2/-  |
|             |                                                                              | " .....                             | 15 c.c.  | 5/-  |
|             |                                                                              | " .....                             | 30 c.c.  | 9/-  |
|             |                                                                              | Bottles .....                       | 120 c.c. | 29/- |
|             | The Capsules                                                                 | Vials (3 minims) .....              | 25       | 2/6  |
|             |                                                                              | " " .....                           | 100      | 8/6  |
|             |                                                                              | " " .....                           | 500      | 33/6 |
|             | <i>Also supplied with Calciferol at same prices.</i>                         |                                     |          |      |
| 50          | <b>HALIBUT OIL OINTMENT</b>                                                  |                                     |          |      |
|             |                                                                              | Pots .....                          | 1 oz.    | 1/6  |
|             |                                                                              | " .....                             | 3 oz.    | 4/-  |
| 44          | <b>HALIMALT (Crookes' Halibut Liver Oil in malt extract)</b>                 |                                     |          |      |
|             |                                                                              | Jars .....                          | 1 lb.    | 2/6  |
|             |                                                                              | " .....                             | 2 lb.    | 4/6  |
|             |                                                                              | " .....                             | 7 lb.    | 12/6 |
| 43          | <b>HALYCALCYNE (Crookes' Halibut Liver Oil with Calcium Phosphate)</b>       |                                     |          |      |
|             | Capsules                                                                     | .....Vials .....                    | 25       | 2/6  |
|             |                                                                              | " .....                             | 100      | 8/6  |
|             |                                                                              | " .....                             | 500      | 33/6 |
| 44          | <b>HALYCITROL (Crookes' Halibut Liver Oil with Orange Juice and Glucose)</b> |                                     |          |      |
|             |                                                                              | Bottles .....                       | 4 oz.    | 2/-  |
|             |                                                                              | " .....                             | 8 oz.    | 3/6  |
|             |                                                                              | " .....                             | 40 oz.   | 15/- |
| 43          | <b>HALIDEXOL (Crookes' Halibut Liver Oil Emulsion)</b>                       |                                     |          |      |
|             |                                                                              | Bottles .....                       | 6 oz.    | 2/-  |
|             |                                                                              | " .....                             | 12 oz.   | 3/6  |
|             |                                                                              | " .....                             | 40 oz.   | 10/- |
| 47          | <b>LACTO-KAOLIN with Vitamin B</b>                                           |                                     |          |      |
|             |                                                                              | Tins (contents by weight) .....     | 4 oz.    | 4/-  |
| 45          | <b>SUPER-D OIL (Crookes)</b>                                                 |                                     |          |      |
|             |                                                                              | Vials (with dropper) .....          | 5 c.c.   | 3/6  |
|             |                                                                              | Capsules (3 minims) Vials .....     | 25       | 4/-  |
| 50          | <b>VITAMIN B<sub>1</sub></b>                                                 |                                     |          |      |
|             | Injection                                                                    | † Ampoules (box of 6) .....         | 1 c.c.   | 7/6  |
|             |                                                                              | Vials .....                         | 30 c.c.  | 14/6 |
| 46          | Oral                                                                         | * Capsules (2 minims) .....         | 25       | 3/-  |
|             |                                                                              | " " .....                           | 100      | 9/6  |
|             |                                                                              | † 1000 International Units per c.c. |          |      |
|             |                                                                              | * Each = 300 International Units.   |          |      |
| 47          | <b>WHEAT GERM OIL</b>                                                        |                                     |          |      |
|             | Capsules                                                                     | Vials of 25 .....                   | —        | 2/6  |

# Laboratories and Special Depots

**GREAT BRITAIN**—THE CROOKES LABORATORIES, Gorst Road, Park Royal, London, N.W.10.

**AUSTRALIA**—Queensland. TAYLORS & ELLIOTTS LTD., Brisbane.  
New South Wales. ELLIOTTS & AUSTRALIAN DRUG LTD., Sydney.  
West Australia. FELTON GRIMWADE & BICKFORD LTD., Perth.  
Victoria. FELTON GRIMWADE & DUERDINS LTD., Melbourne.  
South Australia. A. M. BICKFORD & SONS LTD., Adelaide.  
Tasmania. FELTON GRIMWADE & DUERDINS LTD., Melbourne.

**BARBADOS**—KNIGHTS LTD.

**BURMA**—Rangoon. E. M. DE SOUZA & CO., 465/69 Dalhousie Street.  
GRAND PHARMACY, 438/54 Moghul Street.  
DEY BROTHERS, 290 Moghul Street.

**CANADA**—Ottawa. HEALTH SALES LTD., 52 Nicholas Street.

**CEYLON**—Colombo. MILLER & CO. LTD.  
THE COLOMBO PHARMACY CO. LTD.  
CARGILLS LTD.

**EGYPT**—Cairo. THE EGYPTIAN & BRITISH TRADING CO.,  
Corner Sharia Maghraby and Soliman Pacha.

**FRANCE**—Paris. J. PELOILLE, 2 Rue du Faubourg St. Denis.  
Nice. REILLY & CO., 8 Rue-Niepe.

**GIBRALTAR**—NEW PHARMACY, 159 Main Street.

**INDIA**—Bombay. THE CROOKES LABORATORIES, 10 Graham Road, Ballard Estate.

**IRAQ**—Bagdad. GOURDJI'S WHOLESALE DRUG STORE.  
JOURI & GABBAY DRUG STORE.  
LEVY'S DRUG STORES.

**ITALY**—Milan. I. NURENBERG, Via Zanella 5.

**JAMAICA**—Kingston. ALLAN D. ROBERTS, 10a East Street.

**JAVA**—Bandoeng. BRANDENBURG & PUNT, Apotheek "de Vajzel."

**KENYA**—Nairobi & Mombasa. A. H. WARDLE & CO.

**MALTA**—Valetta. ALFRED GERA & SONS, Economical British Dispensary,  
36 Strada Reale.

**MAURITIUS**—Curepipe. PHARMACY P. BERTULES.  
Port Louis. PHARMACY L. R. PIONORI.  
Rose Hill. P. N. MOREL & CO.

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Customs House Quay.

**PALESTINE**—Tel-Aviv. D. KREISLER, 21 Nachmani.

**PERSIA**—Ispahan. OVKIANOS MARTIN.

**SOUTH AFRICA**—Port Elizabeth. LENNON LTD., P.O. Box 235.

**UGANDA**—Kampala. UGANDA CO., P.O. Box 1.

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Kuala Lumpur. THE FEDERAL DISPENSARY LTD., High Street.  
Singapore. THE MEDICAL HALL LTD., Battery Road.

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